

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions and listings of claims in the application.

Listing of Claims

1.-20. (Canceled).

21. (Withdrawn-Currently Amended) A method of treating or preventing an IMPDH-mediated disease or condition in a mammal comprising the step of administering to said mammal a composition according to any one of claims ~~20, 46~~[[.]] and 50, and 51.

22. (Withdrawn) The method according to claim 21, wherein said IMPDH-mediated disease or condition is selected from transplant rejection, graft versus host disease, or an autoimmune disease.

23. (Withdrawn) The method according to claim 22, wherein said mammal is administered an additional immunosuppressant in a separate dosage form or as part of said composition.

24. (Withdrawn-Currently Amended) A method for inhibiting replication of a virus in a mammal comprising the step of administering to said mammal a composition according to according to any one of claims ~~20, 46~~[[.]] and 50, and 51.

25. (Withdrawn) The method according to claim 24, wherein said virus is selected from orthomyxovirus, paramyxovirus, herpesvirus, retrovirus, flavivirus, pestivirus, hepatotropic virus, bunyavirus, Hantaan virus, Caraparu virus, human papilloma virus, encephalitis virus, arena

virus, reovirus, vesicular stomatitis virus, rhinovirus, enterovirus, Lassa fever virus, togavirus, poxvirus, adenovirus, rubioli, or rubella.

26. (Withdrawn) The method according to claim 25, wherein said mammal is administered an additional anti-viral agent in a separate dosage form or as part of said composition.

27. (Withdrawn-Currently Amended) A method for inhibiting vascular cellular hyperproliferation in a mammal comprising the step of administering to said mammal a composition according to any one of claims 20, 46[.], and 50, ~~and 51~~.

28. (Withdrawn) The method according to claim 27, wherein said method is useful in treating or preventing restenosis, stenosis, arteriosclerosis or other hyperproliferative vascular disease.

29. (Withdrawn) The method according to claim 28, wherein said mammal is administered an additional anti-vascular hyperproliferative agent in a separate dosage form or as part of said composition.

30. (Withdrawn-Currently Amended) A method for inhibiting tumors and cancer in a mammal comprising the step of administering to said mammal a composition according to any one of claims 20, 46[.], and 50, ~~and 51~~.

31. (Withdrawn) The method according to claim 30, wherein said medicament is useful to treat or prevent lymphoma, leukemia and other forms of cancer.

32. (Withdrawn) The method according to claim 31, wherein said mammal is

administered an additional anti-tumor or anti-cancer agent in a separate dosage form or as part of said composition.

33. (Withdrawn-Currently Amended) A method for inhibiting inflammation or an inflammatory disease in a mammal comprising the step of administering to said mammal a composition according to any one of claims ~~20, 46~~ [.,] and 50, and 51.

34. (Withdrawn) The method according to claim 33, wherein said method is useful for treating or preventing osteoarthritis, acute pancreatitis, chronic pancreatitis, asthma or adult respiratory distress syndrome.

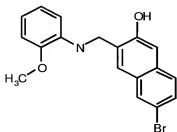
35. (Withdrawn) The method according to claim 33, wherein said mammal is administered an additional anti-inflammatory agent in a separate dosage form or as part of said composition.

36. (Withdrawn-Currently Amended) The composition of claim ~~46 or 20~~, wherein X is $-N(R_6)-C(O)-Y-$.

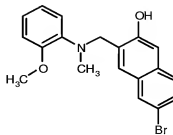
37. (Withdrawn) The composition of claim 36, wherein Y is $-C(R_{12})=C(R_{12})-$.

38. (Withdrawn-Currently Amended) The composition of claim ~~46 or 20~~, wherein Q is $-N(H)-C(O)-O-$.

39. (Withdrawn) A compound selected from the group consisting of 115 and 151;



115



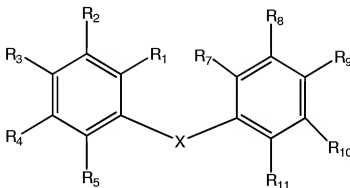
151.

40. (Withdrawn) A compound selected from the group consisting of 101, 103, 104, 105, 106, 107, 110, 111, 112, 113, 114, 116, 117, 118, 119, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 148, 149, 153, 154, 155, 156, 159, 160, 162, 163, 164, 165, 166, 168, 169, 172, 173, 175, 177, 178, 179, 181, 182, 183, 184, 185, 188, 191, 192, 193 and 304.

41.-45. (Canceled).

46. (Previously Presented) A composition comprising:

a) a compound of the formula:



wherein:

X is selected from -C(O)-N(R₆)-, -N(R₆)-C(O)-, -CH₂-N(R₆)-, -N(R₆)-CH₂-,
-N(R₆)-S(O)₂-, -S(O)₂-N(R₆)-, -C(R₁₂)(R₁₂)-C(O)-, -C(O)-C(R₁₂)(R₁₂)-, -C(R₁₂)(R₁₂)-S(O)₂-,
-S(O)₂-C(R₁₂)(R₁₂)-, -S(O)₂-O-, -O-S(O)₂-, -N(R₆)-C(O)-Y- or -Y-C(O)-N(R₆)-; wherein

each R₆ is independently selected from hydrogen, C₁-C₄ straight or branched alkyl,
C₂-C₄ straight or branched alkenyl or alkynyl, Ar-substituted-C₁-C₄ straight or branched alkyl, or
Ar-substituted-C₂-C₄ straight or branched alkenyl or alkynyl; wherein

each R₆, except hydrogen, is optionally substituted with up to 3 substituents
independently selected from halo, hydroxy, nitro, cyano or amino;

each R₁₂ is independently selected from R₆, W-[C₁-C₄ straight or branched alkyl],
W-[C₂-C₄ straight or branched alkenyl or alkynyl], Ar-substituted-[W-[C₁-C₄ straight or branched
alkyl]], Ar-substituted-[W-[C₂-C₄ straight or branched alkenyl or alkynyl]], O-Ar, N(R₆)-Ar, S-Ar,
S(O)-Ar, S(O)₂-Ar, S-C(O)H, N(R₆)-C(O)H, or O-C(O)H; wherein

W is O-, O-C(O)-, S-, S(O)-, S(O)₂-, S-C(O)-, N(R₆)-, or N(R₆)-C(O)-; and wherein

each R₁₂ is optionally and independently substituted with up to 3 substituents
independently selected from halo, hydroxy, nitro, cyano or amino;

Y is selected from -O-, -S-, -C≡C-, -C(R₁₂)₂-C(R₁₂)₂-, -C(R₁₂)₂- or -C(R₁₂)=C(R₁₂)-;

each of R₁, R₂, R₃, R₄, R₅, R₇, R₈, R₉, R₁₀, and R₁₁ is independently selected from
hydrogen, halo, hydroxy, cyano, nitro, amino, -C(O)NH₂, Z-[(C₁-C₄)-straight or branched alkyl],

Z-[(C₂-C₄)-straight or branched alkenyl or alkynyl], Ar-substituted-[(C₁-C₄)-straight or branched alkyl], Ar-substituted-[(C₂-C₄)-straight or branched alkenyl or alkynyl], Ar, Q-Ar, [(C₁-C₄)-straight or branched alkyl]-Q-Ar, [(C₂-C₄)-straight or branched alkenyl or alkynyl]-Q-Ar, O-[(C₁-C₄)-straight or branched alkyl]-Q-Ar, O-[(C₂-C₄)-straight or branched alkenyl or alkynyl]-Q-Ar, [(C₁-C₄)-straight or branched alkyl]-Q-R₁₃, or [(C₂-C₄)-straight or branched alkenyl or alkynyl]-Q-R₁₃,

wherein two adjacent groups selected from either R₁, R₂, R₃, R₄, and R₅ or R₇, R₈, R₉, R₁₀, and R₁₁, are taken together with the carbon atoms to which they are bound to form a 5 to 6 membered aromatic carbocyclic ring or heterocyclic ring; and wherein

Z is selected from a bond, O-, S-, S(O)₂-, C(O)-, OC(O)-, or N(H)C(O)-;

Q is selected from O, -O-C(O)-, -C(O)-O-, -N(H)-C(O)-O-, -O-N(H)-C(O)-, -N(H)-C(O)-, -C(O)-N(H)-, -O-C(O)-N(H)-, or -C(O)-N(H)-O-;

Ar is selected from phenyl, 1-naphthyl, 2-naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, 2-pyrazolynyl, pyrazolidinyl, isoxazolyl, isotriazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazinyl, 1,3,5-trithianyl, indolizynyl, indolyl, isoindolyl, 3H-indolyl, indolinyl, benzo[b]furanyl, benzo[b]thiophenyl, 1H-indazolyl, benzimidazolyl, benzthiazolyl, purinyl, 4H-quinolizynyl, quinolynyl, isoquinolynyl, 1,2,3,4-tetrahydro-isoquinolynyl, cinnolynyl, phthalazinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, piperidinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl or phenoxazinyl or other chemically feasible monocyclic, bicyclic or

tricyclic ring systems, wherein each ring consists of 5 to 7 ring atoms and wherein each ring comprises 0 to 3 heteroatoms independently selected from N, O and S;

R_{13} is selected from [C_1 - C_{12} straight or branched alkyl] or, [C_2 - C_{12} straight or branched alkenyl or alkynyl]; wherein R_{13} is optionally substituted with 1 to 4 substituents independently selected from R_{14} or R_{15} , wherein

each R_{14} is a monocyclic or a bicyclic ring system consisting of 3 to 7 members per ring, wherein said ring system optionally comprises up to 4 heteroatoms selected from N, O, and S; wherein a CH_2 adjacent to said N, O or S may be substituted with C(O); and wherein R_{14} optionally comprises up to 2 substituents independently selected from (C_1 - C_4)-straight or branched alkyl, (C_2 - C_4)-straight or branched alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, $(CH_2)_n$ - R_{16} , -S- $(CH_2)_n$ - R_{16} , -S(O)- $(CH_2)_n$ - R_{16} , -S(O) $_2$ - $(CH_2)_n$ - R_{16} , -O- $(CH_2)_n$ - R_{16} , or -N(R_{18})- $(CH_2)_n$ - R_{16}

wherein n is 0, 1 or 2;

R_{16} is selected from halogen, -CN, -NO $_2$, -CF $_3$, -OCF $_3$, -OH, -S- $(C_1$ - C_4)-alkyl, -S(O)- $(C_1$ - C_4)-alkyl, -S(O) $_2$ - $(C_1$ - C_4)-alkyl, -NH $_2$, -NH- $(C_1$ - C_4)-alkyl, -N($(C_1$ - C_4)-alkyl) $_2$, COOH, C(O)-O- $(C_1$ - C_4)-alkyl or O- $(C_1$ - C_4)-alkyl; and

each R_{15} is independently selected from -OR $_{17}$, or -N(R_{18}) $_2$;

R_{17} is selected from hydrogen, - $(C_1$ - C_6)-straight alkyl, - $(C_1$ - C_6)-straight alkyl-Ar, -C(O)- $(C_1$ - C_6)-straight or branched alkyl, -C(O)-Ar, or - $(C_1$ - C_6)-straight alkyl-CN; and

each R_{18} is independently selected from - $(C_1$ - C_6)-straight or branched alkyl,

-(C₁-C₆)-straight or branched alkyl-Ar, -(C₁-C₆)-straight alkyl-CN, -(C₁-C₆)-straight alkyl-OH,
-(C₁-C₆)-straight alkyl-OR₁₇, -C(O)-(C₁-C₆)-straight or branched alkyl, -C(O)-Ar,
-S(O)₂-(C₁-C₆)-straight or branched alkyl, or -S(O)₂-Ar; wherein

any alkyl, alkenyl or alkynyl group is optionally substituted with 1 to 3
independently selected halo groups; and

any Ar, aromatic carbocyclic ring or heterocyclic ring is optionally substituted with
1 to 3 substituents independently selected from halo, hydroxy, nitro, cyano, amino, (C₁-C₄)-straight
or branched alkyl; O-(C₁-C₄)-straight or branched alkyl, (C₂-C₄)-straight or branched alkenyl or
alkynyl, or O-(C₂-C₄)-straight or branched alkenyl or alkynyl;

any Ar, aromatic carbocyclic ring or heterocyclic ring is optionally benzofused;
with the provisos that:

at least two of R₁, R₂, R₃, R₄, or R₅ is hydrogen;

no more than two of R₁, R₂, R₃, R₄, or R₅ comprises Ar;

at least two of R₇, R₈, R₉, R₁₀ or R₁₁ is hydrogen; and

no more than two of R₇, R₈, R₉, R₁₀ or R₁₁ comprises Ar; and

when X is -C(O)-NH- or -NH-C(O)-, any two adjacent groups selected from R₁, R₂,
R₃, R₄, and R₅ are taken together with the carbon atoms to which they are bound to form an
unsubstituted fused benzene ring, the remaining three of R₁, R₂, R₃, R₄, and R₅ are one hydroxy
group and two hydrogen groups, and four of R₇, R₈, R₉, R₁₀, and R₁₁ are hydrogen, then the

remaining one of R₇, R₈, R₉, R₁₀, and R₁₁ is not 2-(4-chloro-phenyl)-ethyl, 2-(3,4-dichloro-phenyl)ethyl, 2-(3,4-dimethoxy-phenyl)ethyl, or 2-(1,1'-biphenyl-4-yl)ethyl; and

when X is -C(O)-NH- or -NH-C(O)-, any two adjacent groups selected from R₇, R₈, R₉, R₁₀, and R₁₁ are taken together with the carbon atoms to which they are bound to form an unsubstituted fused benzene ring, the remaining three of R₇, R₈, R₉, R₁₀, and R₁₁ are one hydroxy group and two hydrogen groups, and four of R₁, R₂, R₃, R₄, and R₅ are hydrogen, then the remaining one of R₁, R₂, R₃, R₄, and R₅ is not 2-(4-chlorophenyl)-ethyl, 2-(3,4-dichlorophenyl)ethyl, 2-(3,4-dimethoxy-phenyl)ethyl, or 2-(1,1'-biphenyl-4-yl)ethyl;

when X is -SO₂-NH- or -NH-SO₂-, one of R₁, R₂, R₃, R₄, and R₅ is -NH₂, the remaining four of R₁, R₂, R₃, R₄, and R₅ are hydrogen, and any two adjacent groups selected from R₇, R₈, R₉, R₁₀, and R₁₁ are taken together with the carbon atoms to which they are bound to form an unsubstituted pyridine ring fused to a benzene ring, then at least one of the remaining R₇, R₈, R₉, R₁₀, and R₁₁ is not hydrogen or -OCH₃;

when X is -SO₂-NH- or -NH-SO₂-, one of R₇, R₈, R₉, R₁₀, and R₁₁ is -NH₂, the remaining four of R₇, R₈, R₉, R₁₀, and R₁₁ are hydrogen, and any two adjacent groups selected from R₁, R₂, R₃, R₄, and R₅ are taken together with the carbon atoms to which they are bound to form an unsubstituted pyridine ring fused to a benzene ring, then at least one of the remaining R₁, R₂, R₃, R₄, and R₅ is not hydrogen or -OCH₃;

when X is -SO₂-NH- or -NH-SO₂- and four of R₁, R₂, R₃, R₄, and R₅ are hydrogen, then any two adjacent groups selected from R₇, R₈, R₉, R₁₀, and R₁₁ are not taken together with the carbon atoms to which they are bound to form an unsubstituted indole ring, an indole ring

substituted by -Cl, =O, -cyano, -CH₃, or -C(O)-CH₃, or an unsubstituted indazole ring; and

when X is -SO₂-NH- or -NH-SO₂- and four of R₇, R₈, R₉, R₁₀, and R₁₁ are hydrogen, then any two adjacent groups selected from R₁, R₂, R₃, R₄, and R₅ are not taken together with the carbon atoms to which they are bound to form an unsubstituted indole ring, an indole ring substituted by -Cl, =O, -cyano, -CH₃, or -C(O)-CH₃, or an unsubstituted indazole ring; and

b) a carrier, adjuvant or vehicle, which is pharmaceutically acceptable for oral administration or administration by injection.

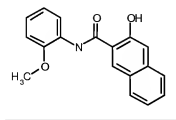
47. (Canceled).

48. (Currently Amended) The composition according to claim 46 ~~or 20~~, wherein X is -N(H)-C(O)- or -C(O)-N(H)-.

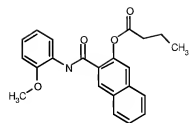
49. (Canceled).

50. (Currently Amended) A composition comprising:

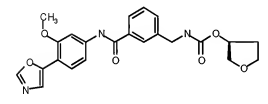
a) a compound selected from the group consisting of: ~~400, 401, 402, 403, 404, 405, 406, 407, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 448, 449, 451, 452, 453, 454, 455, 456, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 475, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 490, 491, 492, 493, 496, 200, 204, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, and 326;~~



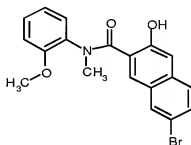
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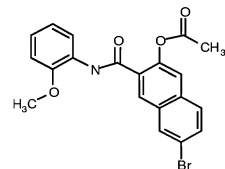
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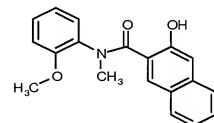
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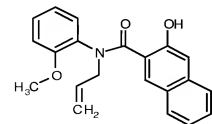
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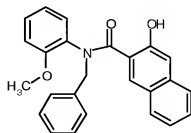
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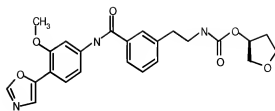
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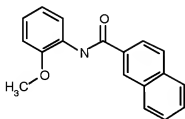
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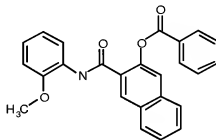
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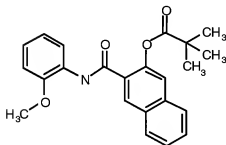
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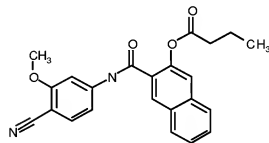
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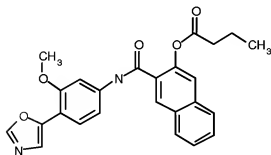
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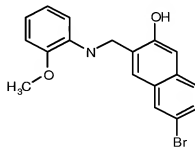
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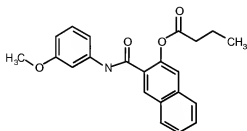
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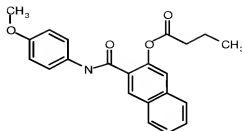
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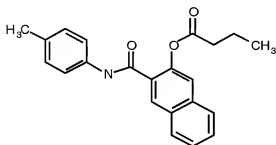
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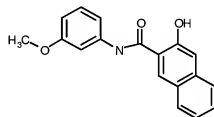
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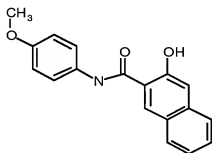
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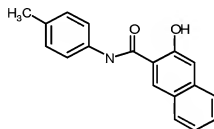
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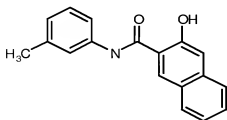
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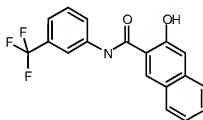
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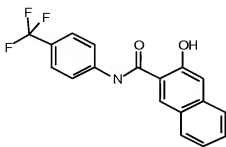
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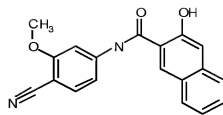
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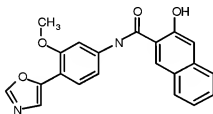
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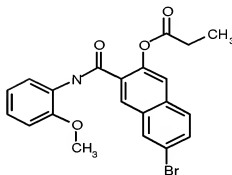
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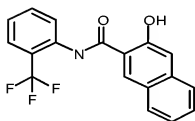
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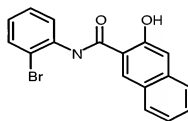
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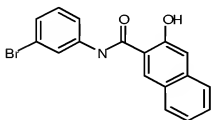
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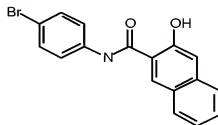
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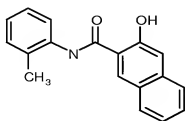
129



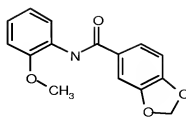
130



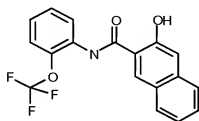
131



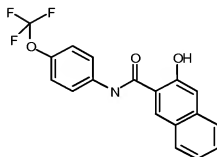
132



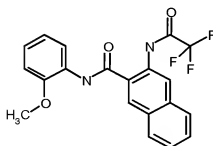
134



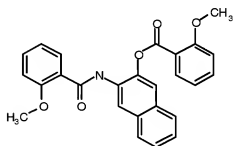
135



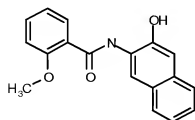
136



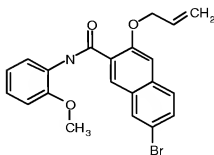
137



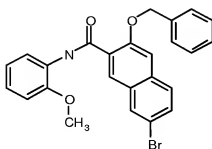
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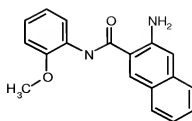
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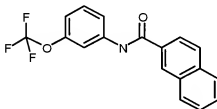
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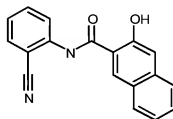
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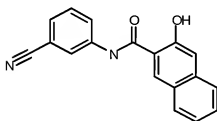
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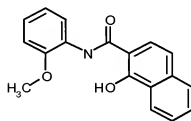
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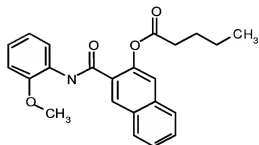
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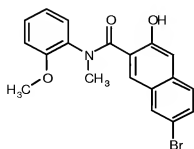
145



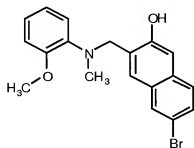
146



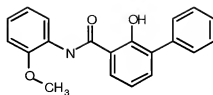
148



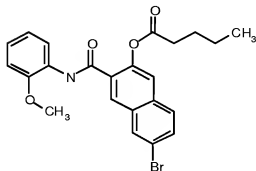
149



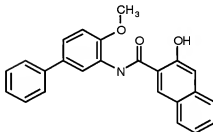
151



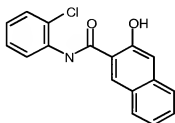
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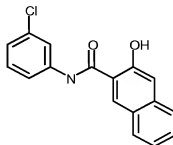
153



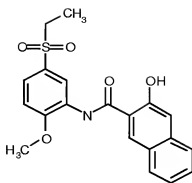
154



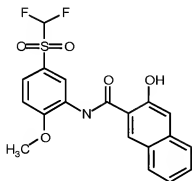
155



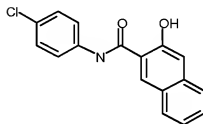
156



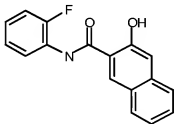
159



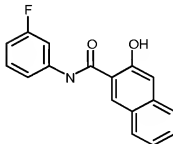
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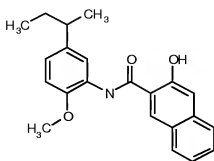
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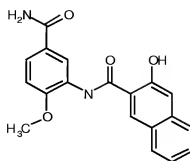
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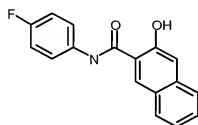
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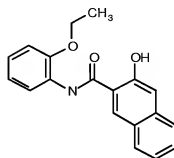
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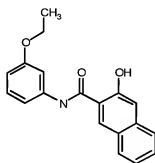
165



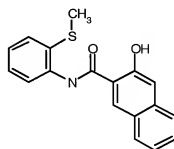
166



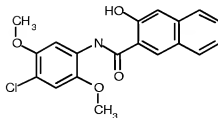
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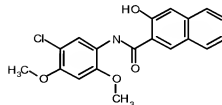
168



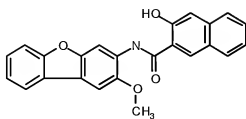
169



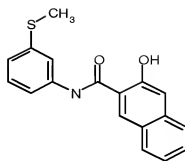
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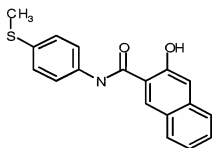
171



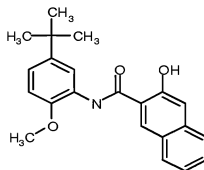
172



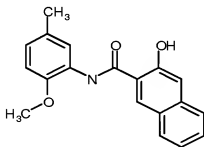
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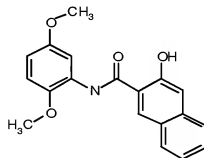
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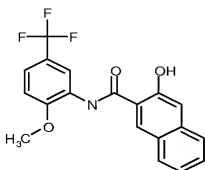
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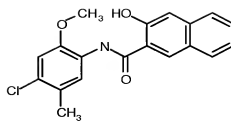
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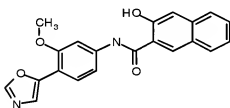
179



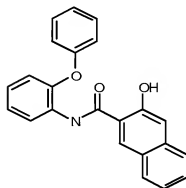
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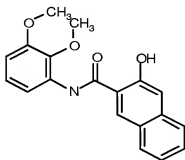
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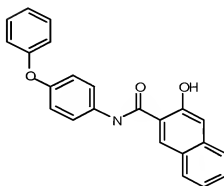
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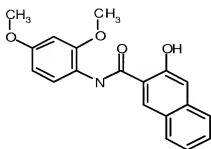
183



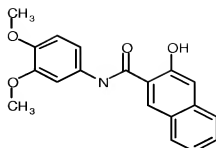
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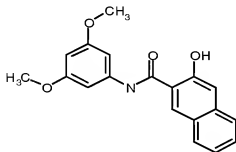
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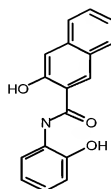
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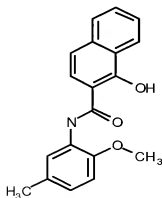
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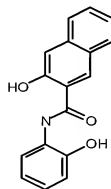
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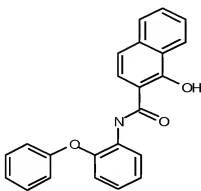
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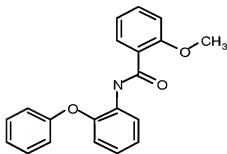
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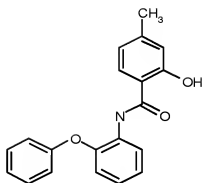
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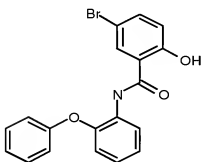
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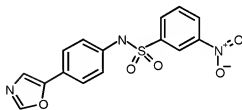
196



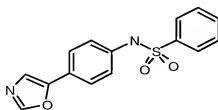
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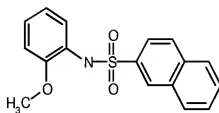
204



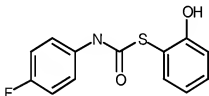
300



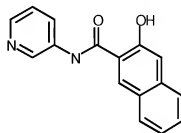
301



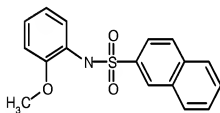
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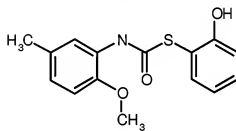
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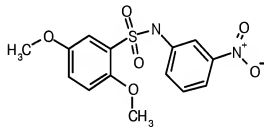
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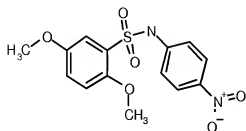
305



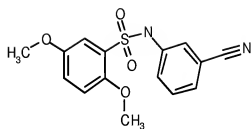
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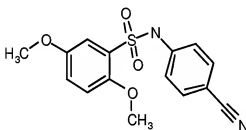
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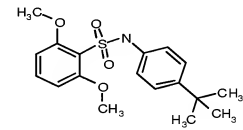
308



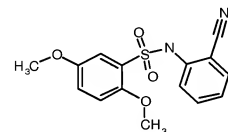
309



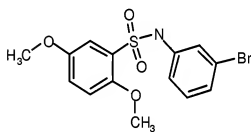
310



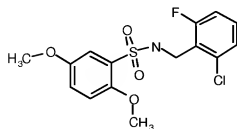
311



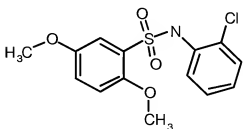
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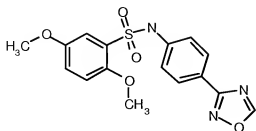
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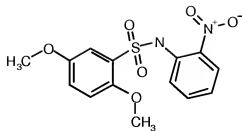
314



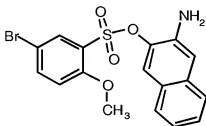
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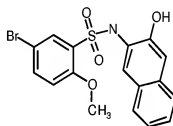
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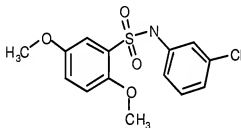
317



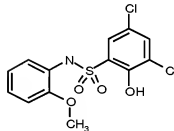
318



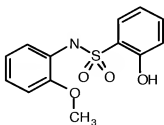
319



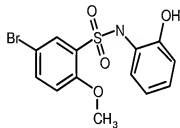
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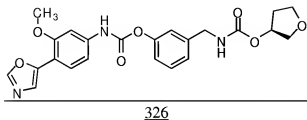
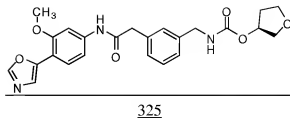
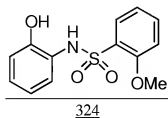
321



322



323



and

b) a carrier, adjuvant, or vehicle, which is pharmaceutically acceptable for oral administration or administration by injection.

51. (Canceled).